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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/714,333	11/14/2003	Anastasia Khvorova	DHARMA 0100-US2	6379

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EXAMINER	
PITRAK, JENNIFER S	
ART UNIT	**PAPER NUMBER**
1635	
MAIL DATE	**DELIVERY MODE**
10/29/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/714,333	KHVOROVA ET AL.	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-54,57-60,68,70-77,79,81,84-87 and 92-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-54, 57-60, 68, 70-77, 79, 81, 84-87, and 92-99* is/are rejected.

7)☒ Claim(s) *57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/15/2010(2)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 09/15/2010 has been entered. Rejections and/or objections not reiterated from the previous office action mailed 03/16/2010 are hereby withdrawn. The rejections and/or objections presented herein are either newly applied or are reiterated and are the only rejections and/or objections currently outstanding.

Claims 43-54, 57-60, 68, 70-77, 79, 81, 84-87, and 92-99 are pending and are under examination.

Claim Objections

Claim 57 is objected to because of the following informalities: the claim requires the following two criteria: 1) the presence of A at position 19 of the sense sequence and 2) the absence of C at position 19 of the sense sequence. Criterion 2 does not further limit the claim in light of criterion 1. Claim 57 is also objected to because the claim recites "said siRNA sequence that is selected for said target gene", which lacks specific antecedent basis. This phrase would

more appropriately read "said siRNA sequence for the target gene". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-54, 57-60, 68, 70-77, 79, 81, 84-87, and 92-99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 43 recites the limitation "the sense region" in lines 17-21. There is insufficient antecedent basis for this limitation in the claim.

Claim 52 recites the limitation "the candidate siRNA" in the first line on page 4 of Applicant's 09/15/2010 submission. There is insufficient antecedent basis for this limitation in the claim.

Claim 68 recites the limitation "the sense region" in lines 18-22. There is insufficient antecedent basis for this limitation in the claim.

Claim 68 recites the limitation "said siRNA sequence for the target gene" in line 24. There is insufficient antecedent basis for this limitation in the claim.

Claim 86 recites the limitation "said sequence" in line 1 on page 9 of Applicant's 09/15/2010 response. There is insufficient antecedent basis for this limitation in the claim.

Claim 86 recites the limitation "the sense region" in lines 2-5 on page 9 of Applicant's 09/15/2010 response. There is insufficient antecedent basis for this limitation in the claim.

Claim 86 recites the limitation "said siRNA molecule for said target gene" in line step (e) of claim 86. There is insufficient antecedent basis for this limitation in the claim.

Claims 92-94 are indefinite because the claims require that each candidate siRNA sequence is 100% complementary to a region of the target gene. This limitation contradicts the limitation of the independent base claims (claims 43, 68, and 86, respectively) that each candidate siRNA sequence comprises a sense sequence that is at least 90% similar to a region of a target gene. Therefore the entire candidate siRNA sequence cannot possibly be 100% complementary to a region of the target gene. Furthermore an siRNA molecule comprises complementary strands such that reference to an "siRNA sequence" is ambiguous with regard to whether it refers to the sense, antisense, or both strands of the siRNA molecule.

Claims 97, 98, and 99 recite the limitation "the sense region". There is insufficient antecedent basis for this limitation in the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 43, 48, 52, 68, 74, 79, 81, 84, 85, 92, 93, 95, 97, and 98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elbashir, et al. (2002, Methods, v.26: 199-213, of record, 09/05/2007 Office Action).

Elbashir, et al. teach a method comprising 1) selecting siRNA sequences meeting the criterion of an absence of C at position 19 of the sense sequence and a G/C content of about 50% and 2) synthesizing siRNAs meeting these criteria (see page 202, left column). The siRNA sequences have sense sequences that are 100% identical to the target mRNA sequence and antisense strands that are 100% complementary to the sense strand sequence. Elbashir, et al. teach that the siRNAs are preferably chemically synthesized (page 202, second paragraph in right column). Elbashir, et al. does not teach selecting siRNAs by using a computer to apply an algorithm containing the aforementioned criteria. Elbashir, et al. does not teach synthesizing siRNAs via enzymatic synthesis.

It would have been obvious to automate the method taught by Elbashir, et al. such as by using a computer to apply an algorithm comprising the aforementioned criteria because such automation is easily obtained by those of skill in the art and is more efficient that applying the criteria manually. It further would have been obvious to one of skill in the art to synthesize the siRNAs by any reasonable means known to those of skill in the art, which includes enzymatic synthesis. Therefore, the instant claims would have been *prima facie* obvious to those of skill in the art at the time the instant invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10/940892

Claims 43-46, 48, 51, 52, 53, 54, 68, 70, 71, 72, 74, 77, 79, 81, 84, 85, 86, 87, 92, 93, 94, 95, 96, 97, 98, and 99 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 67-86 of copending Application No. 10/940892. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the instant claims and the '892 claims significantly overlap. The instant claims and the '892 claim are directed to methods for obtaining an siRNA for a target gene comprising applying, via computer algorithm, common criteria regarding sequence content of candidate siRNA sequences.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12/802647

Claims 43-54, 57-60, 68, 70-77, 79, 81, 84-87, and 92-99 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-31 of copending Application No. 12/802647. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the instant claims and the '647 claims significantly overlap. The instant claims and the '647 claim are directed to methods for obtaining an siRNA for a target gene comprising applying, via computer algorithm, common criteria regarding sequence content of candidate siRNA sequences by assessing the presence or absence of particular nucleotides at particular positions within siRNA sense sequences.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jennifer Pitrak/
Examiner, Art Unit 1635